Reviewer's report

**Title:** Thymidylate Synthase, Dihydropyrimidine Dehydrogenase, ERCC1, and Thymidine Phosphorylase Gene Expression in Primary and Metastatic Gastrointestinal Adenocarcinoma Tissue in Patients Treated on a Phase I Trial of Oxaliplatin and Capecitabine

**Version:** 1  **Date:** 19 March 2008

**Reviewer:** Daniela Aust

Reviewer's report:

The manuscript "Thymidylate Synthase, Dihydropyrimidine Dehydrogenase, ERCC1, and Thymidine Phosphorylase Gene Expression in Primary and Metastatic Gastrointestinal Adenocarcinoma Tissue in Patients Treated on a Phase I Trial of Oxaliplatin and Capecitabine" reports the RNA expression in fresh frozen biopsies of gastrointestinal tumor metastases and compares this RNA expression to the RNA expression of the primary tumors. The material derives from a Phase I trial in metastatic gastrointestinal cancer (n=81).

**Major Compulsory Revisions**

1. The authors state that the median mRNA levels are higher in the metastases than in the primary tumors and explain this finding with a long interval from initial diagnosis to study entry. That is probably not the explanation. The explanation is rather that mRNA expression in FFPE samples (primary tumors) is compared to mRNA expression in FF samples (metastases). This would also explain the greater variability of the measurements in the primary tumors. The authors have to clearly state that in the discussion and cite the appropriate literature.

2. The measurements of mRNA expression are not corroborated by protein expression analyses (e.g. IH). This should be done to strengthen the findings.

3. The manuscript does not offer any new aspects on the four target genes investigated other than the samples deriving from a prospective study.

**Minor Essential Revisions**

4. The definition of "time to treatment failure" seems somewhat problematic since it also includes patient withdrawal from the study which may not be due to disease progression but other causes (toxicity, etc). This needs to be clarified and the correlation with pure disease progression needs to be stated.

**Discretionary Revisions**

5. The primers for real time PCR should be given in a table rather than in the text.

6. There are a few typographical errors (page 6, page 12, second paragraph).

All in all, the manuscript is not acceptable for publication in its present state. It needs major revision. The impact on the knowledge about the studied genes is
rather low.